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CASE REPORT

Successful treatment of systemic lupus erythematosus with subcutaneous immunoglobulin

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The therapeutic efficacy of high-dose intravenous immunoglobulin in systemic lupus erythematosus (SLE) patients is well established. However, side effects might limit its use and lead to the consideration of therapeutic alternatives, such as the subcutaneous formulation of immunoglobulin, which has been used in some patients with other autoimmune diseases. We report a case of SLE refractory to classical therapies. High-dose intravenous immunoglobulin was effective, but gave rise to significant side effects. The patient was successfully treated with subcutaneous human immunoglobulin, achieving and maintaining clinical and laboratory remission. A lower immunoglobulin dose was needed and no side effects were observed, compared to the intravenous administration. Subcutaneous immunoglobulin could be a better-tolerated and cost-saving therapeutic option for select SLE patients. *Lupus* (2016) **25,** 663–665.

Key words: Systemic lupus erythematosus; cutaneous lupus; discoid lupus

Introduction

High-dose intravenous human immunoglobulin (IvIg) has been shown to significantly reduce disease activity in systemic lupus erythematous (SLE) patients,[1] increase complement levels[1] and to be effective in hematologic and cardiac involvement.[2] It also decreases disease activity, as well as frequency and severity of relapses in cutaneous lupus patients.[3] Immediate infusion-related side effects have been reported to occur in 1%–8% of IvIg perfusions.[4] Those are probably related to immunoglobulin peak serum concentration[4] and might limit its use in some patients.

Subcutaneous administration of human immunoglobulin (ScIg) is well known as replacement therapy in primary immunodeficiency, for which lower doses are needed.[5] Some authors have also reported effectiveness of ScIg therapy in inflammatory myopathies and neuropathic diseases.[6] However, it has been proposed that modifying immunoglobulin dose and route of administration could change its interaction with the immune system.[6] Therefore, it is not known whether ScIg has the same effects and indications as IvIg. In a literature review, we could not find any case report or series of SLE patients treated with ScIg.

Case report

A 52-year-old Caucasian woman was diagnosed with SLE more than 10 years ago. She presented with extensive cutaneous involvement and histologically proven subacute cutaneous lupus and later developed typical discoid plaques on photo-exposed areas (Figure 1) and peripheral vasculopathy lesions (Figure 2). The patient also complained of asthenia, polyarthritis, Raynaud's phenomenon and sicca symptoms. Blood tests were remarkable for positive antinuclear antibodies (1/320), anti-double-stranded DNA (anti-dsDNA) and anti-SSA and low C3 levels. Antiphospholipid antibodies were negative. No renal or haematologic involvement was observed during disease course.

She has been treated over the last decade with intermittent topical corticosteroids and calcineurin

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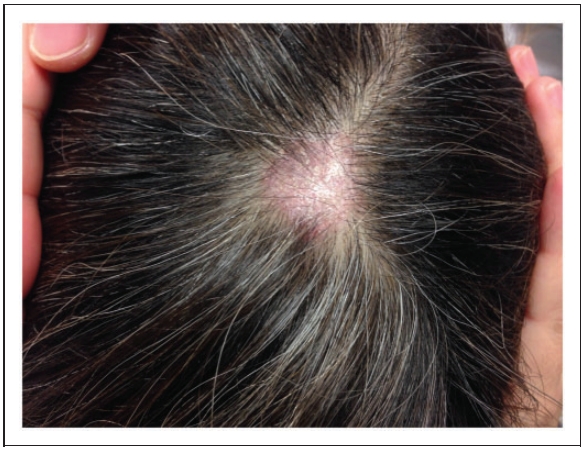

Figure 1 Discoid lesion on the scalp.

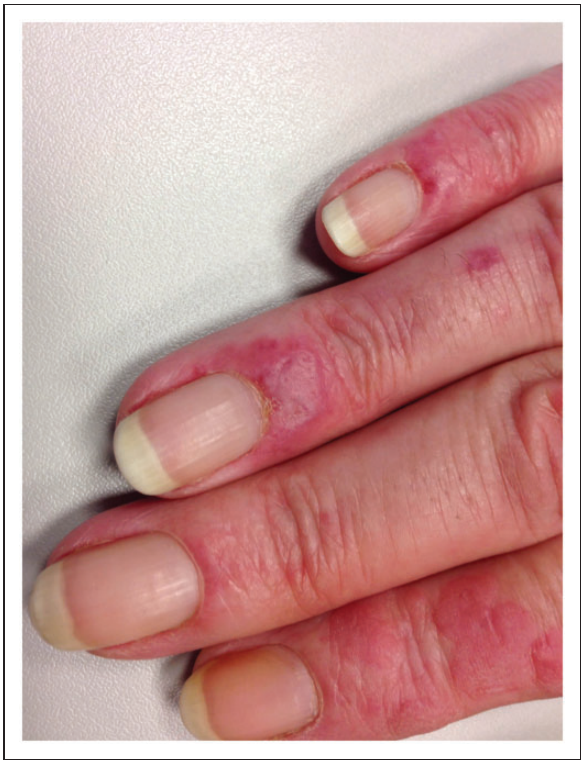

Figure 2 Erythemato-violaceous periungual plaques.

inhibitors, low-dose systemic corticosteroids, hydroxychloroquine and azathioprine. Methotrexate was not tolerated because of gastrointestinal side effects. Due to poor disease control, namely new onset of cutaneous rash, lupus vasculitis and low C3 levels (0.61 g/l; laboratory reference value >0.90 g/l), scored as 12 on the Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index[7] (SELENA-SLEDAI), it was decided to associate IvIg 2 g/Kg administered over two days every four weeks (dose per cycle = 134 g). After the second cycle, a marked clinical improvement was evident, but the patient experienced extremely intense and incapacitating headache, dizziness and emesis during and after each treatment, even with a lower infusion rate (divided over four days) and premedication with an antihistamine. IvIg treatment was suspended after the fourth cycle. Clinical worsening occurred a few weeks later and it was decided to start treatment with ScIg preceded by an IvIg cycle (2 g/Kg) in order to achieve therapeutic levels. These were afterwards maintained with 8.25 g of ScIg (Gammanorm® 0.165 g/ml), three times per week infused at 20–30 ml/hour by two portable pumps during a two- to three-hour period. The first three administrations were performed at the hospital, and treatment was continued on a home-based self-administration thereafter. Complete clinical response was achieved and maintained over 18 months of ScIg treatment. The patient then decided to discontinue ScIg administration and some weeks later a clinical flare was observed, with an increase of SELENA-SLEDAI score to 10. Restarting ScIg at the same dose did not control disease activity. After another cycle of IvIg followed by the same dose of ScIg, complete clinical remission was achieved without adverse effects. The patient is currently in clinical and laboratory remission on ScIg twice weekly (total Ig monthly dose = 66 g), with a SELENA-SLEDAI score of 2 (slight hypocomplementemia – C3 0.79 g/l).

Discussion

We report the case of an SLE patient who clinically benefited from IvIg therapy, but was not able to tolerate it due to significant side effects. Low-dose subcutaneous immunoglobulin (approximately 100 g/month corresponding to 1.5 g/Kg/month with further reduction to 66 g/month, equivalent to 1 g/Kg/month) was then administered successfully, both in terms of efficacy and tolerability.

To the best of our knowledge, ScIg for immunomodulatory purposes in SLE patients has not been previously reported. Our case suggests that it may be a valid, cost-saving therapeutic option for some patients, maintaining efficacy with a total lower dose and favourable safety profile when compared to IvIg. The administration can be performed at home, saving hospital associated-costs and diminishing work absenteeism.

Moreover, serum levels of immunoglobulin are more stable when administered subcutaneously. Patients who are symptomatic between IvIg cycles might benefit from this pharmacokinetic property of ScIg.

However, the dose of immunoglobulin that can be delivered through the subcutaneous route is limited to 100 g/month, making this approach unsuitable for overweight patients. It also requires a preceding IvIg cycle, with associated costs and side effects.

Similarly to what has been reported for inflammatory myopathy patients, ScIg can also be attempted in SLE patients for whom other therapeutic options, such as rituximab or belimumab, are not available or indicated. Controlled studies are needed in order to better understand the role of ScIg in SLE patients.

Declaration of Conflicting Interests

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